Amendments to the Specification

Please amend the paragraph on page 1, immediately after the heading "CROSS-REFERENCE TO RELATED APPLICATIONS" to reads as follows:

This application is a divisional application of U.S. Patent Application Serial No. 09/272,835 filed March 19, 1999, which claims the benefit under 35 U.S.C. 119(e) of Provisional Applications Serial No. 60/079,124, filed March 23, 1998, and Serial No. 60/081,569, filed April 13, 1998, from which non-provisional patent application priority is claimed under 35 U.S.C. 120, the entire contents of which provisional and non-provisional applications are hereby incorporated by reference.

Please amend the paragraph beginning at page 3, line 16 to read as follows:

In one embodiment, the invention provides an isolated nucleic acid molecule having at least about 65% sequence identity to (a) a nucleic acid sequence encoding a GFRα3 polypeptide comprising the sequence of amino acids 27 to 400 of SEQ ID NO: 15, amino acids 27 to 369 of SEQ ID NO: 17 or amino acids 27 to 374 of SEQ ID NO: 5 or (b) the complement of the nucleic acid molecules of (a). In another embodiment, the nucleic molecule sequence above comprises a ligand-binding domain of a GFRα3 polypeptide of amino acids 84 to 360 of SEQ ID NO: 15, amino acids 84 to 329 of SEQ ID NO: 17, or the sequence of amino acids 110 to 386 of SEQ ID NO: 20, or their complementary nucleic acids. The isolated nucleic acid comprises a GFRα3 encoding sequence which preferably hybridizes under stringent conditions to nucleic acid sequences encoding a GFRα3 polypeptide of the invention. The sequence identity preferably is at least about 75%, more preferably at least 85%, even more preferably at least 90%, most preferably at least 95%. In one aspect, the encoded polypeptide has at least about 75%, preferably at least 80%, more preferably at least 85%, even more preferably at least 90%, and most preferably at least about 95% sequence identity with a polypeptide having amino acid residues 27 to 400 of SEQ ID NO: 15, amino acids 27 to 369 of SEQ ID NO: 17, amino acids 27 to 374 of SEQ ID NO: 5, a ligand-binding domain of a GFRα3 polypeptide of amino acids 84 to 360 of SEQ ID NO: 15, amino acids 84 to 329 of

SEQ ID NO: 17, or the sequence of amino acids 110 to 386 of SEQ ID NO: 20. Preferably the identity is to amino acid residues 27 to 400 of SEQ ID NO: 15 and DNA encoding it. In a further embodiment, the isolated nucleic acid molecule comprises DNA encoding a GFRα3 polypeptide having amino acid residues 27 to 400 of SEQ ID NO:15, or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the invention provides a nucleic acid of the full length protein of clone DNA48613 (SEQ ID NO: 14), DNA48614 (SEQ ID NO: 16) or murine GFRα3 (SEQ ID NO: 4, clone 13). DNA48613-1268 (SEQ ID NO: 14) and DNA48614-1268 SEQ ID NO: 16) were deposited with the ATCC under accession numbers ATCC 209752 (Designation: DNA48613-1268) and ATCC 209751 (Designation: DNA48614-1268) ~~and ATCC _____~~, respectively, on Apr. 07, 1998.

Please amend the paragraph beginning at page 7, line 23 to read as follows:

Figures 1A-B ~~shows~~ show the nucleotide sequence (SEQ ID NO: 4) and deduced amino acid sequence (SEQ ID NO: 5) of a native sequence of murine GFRα3.

Please amend the paragraph beginning at page 7, line 30 to read as follows:

Figure 3 shows the alignment comparison between murine (SEQ ID NO: 5) and human (SEQ ID NO: 15) GFRα3 amino acid sequences. Conserved residues are boxed.

On page 7, please amend the paragraph beginning at line 32 to read as follows:

Figure 4 shows the alignment comparison between human GFRα3 (SEQ ID NO: 15 from DNA48613) and its splice variant (SEQ ID NO: 17 from DNA48614).

Conserved sequences are boxed. The 30 amino acid deletion sequence is indicated.

Please amend the paragraph beginning at page 7, line 35 to read as follows:

Figures 5A-B ~~shows~~ show the nucleic acid sequence alignment of the DNA sequence (SEQ ID NO: 14) encoding human GFRα3 with DNAs ~~(SEQ ID NO: 21 and SEQ ID NO:22)~~ encoding human GFRα1 (SEQ ID NO: 6) and human GFRα2 (SEQ ID NO: 7), respectively.

Please amend the paragraph beginning at page 17, line 33 and ending at page 18, line 10, as follows:

Glial cell line-derived neurotrophic ~~facros~~ factor ("GDNF") (Lin *et al., Science,* 260:1130-1132 (1993); WO 93/06116, which are incorporated herein in its entirety), is a potent survival factor for midbrain dopaminergic (Lin *et al.,*~~Science, 260:1130-1132~~ (1993), *supra*; Strömberg *et al., Exp. Neurol.*, 124:401-412 (1993); Beck *et al., Nature*, 373:339-341 (1995): Kearns *et al., Brain Res.*, 672:104-111 (1995); Tomac *et al., Nature,* 373:335-339 (1995)), spinal motor (Henderson *et al., Science*, 266:1062-1064 (1994); Oppenheim *et al., Nature,* 373:344-346 (1995)~~)~~; Yan *et al., Nature,* 373:341-344 (1995)), and noradrenergic neurons (Arenas *et al., Neuron*, 15:1465-1473 (1995)), which degenerate in Parkinson's disease (Hirsch *et al., Nature,* 334:345-348 (1988): Hornykiewicz, *Mt. Sinai J. Med.,* 55:11-20 (1988)), amyotrophic lateral sclerosis (Hirano, Amyotrophic Lateral Sclerosis and Other Motor Neuron Disease, P. Rowland, ed. (New York: Raven Press, Inc.) pp. 91-101 (1991), and Alzheimer's disease (Marcyniuk *et al., J. Neurol. Sci.,* 76:335-345 (1986); Cash *et al., Neurology,* 37:42-46 (1987); Chan-Palay *et al., Comp. Neurol.*, 287:373-392 (1989)), respectively. Based on mice genetically engineered to lack GDNF, additional biological roles for GDNF have been reported: the development and/or survival of enteric, sympathetic, and sensory neurons and the renal system, but not for catecholaminergic neurons in the central nervous system (CNS) (Moore *et al.,*

Nature 382:76-79 (1996); Pichel *et al., Nature* 382:73-76 (1996); Sanchez *et al., Nature* 382:70-73 (1996)). Despite the physiological and clinical importance of GDNF, little is known about its mechanism of action.

Please amend the paragraph beginning at page 19, line 16 as follows:

The variants can be those encoded by an isolated nucleic acid molecule having at least about 65% sequence identity to (a) a nucleic acid sequence encoding a GFRα3 polypeptide comprising the sequence of amino acids 27 to 400 of SEQ ID NO: 15, amino acids 27 to 369 of SEQ ID NO: 17 or amino acids 27 to 374 of SEQ ID NO: 5 or (b) the complement of the nucleic acid molecules of (a). Further, the variants can be encoded by nucleic molecule sequences comprising a ligand-binding domain of a GFRα3 polypeptide of amino acids 84 to 360 of SEQ ID NO: 15, amino acids 84 to 329 of SEQ ID NO: 17, or the sequence of amino acids 110 to 386 of SEQ ID NO: 20, or their complementary nucleic acids. These isolated nucleic acid molecules preferably comprise a GFRα3 encoding sequence which preferably hybridizes under stringent conditions to nucleic acid sequences encoding a GFRα3 polypeptide of the invention. The sequence identity preferably is at least about 75%, more preferably at least 85%, even more preferably at least 90%, most preferably at least 95%. Typically, the polypeptide has at least about 75%, preferably at least 80%, more preferably at least 85%, even more preferably at least 90%, and most preferably at least about 95% sequence identity with a polypeptide having amino acid residues 27 to 400 of SEQ ID NO: 15, amino acids 27 to 369 of SEQ ID NO: 17, amino acids 27 to 374 of SEQ ID NO: 5, a ligand-binding domain of a GFRα3 polypeptide of amino acids 84 to 360 of SEQ ID NO: 15, amino acids 84 to 329 of SEQ ID NO: 17, or the sequence of amino acids 110 to 386 of SEQ ID NO: 20. Preferably the identity is to amino acid residues 27 to 400 of SEQ ID NO: 15 and DNA encoding it. The isolated nucleic acid molecule can contain a DNA encoding a GFRα3 polypeptide having amino acid residues 27 to 400 of SEQ ID NO: 15, or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The protein can be encoded by the nucleic acid encoding the full length protein of clone DNA48613, DNA48614 or murine GFRα3 (clone 13), or one that hybridizes thereo

under stringent conditions. DNA48613 (SEQ ID NO: 14) and DNA 48614 (SEQ ID NO: 16) were deposited with the ATCC under accession numbers ATCC 209752 (Designation: DNA48613-1268), ATCC 209751 (Designation: DNA48614-1268), ~~and ATCC _____~~, respectively, on Apr. 7, 1998~~, or one that hybridizes thereto under stringent conditions~~.

Please amend the paragraph beginning at page 49, line 9 as follows:

The deduced amino acid sequence (SEQ ID NO: 17) of DNA48614 and comparison to SEQ ID NO: 15, revealed it to be an alternatively spliced form of DNA48613, with a 30 amino acid deletion (amino acid positions 127-157, counting from the initiation methionine), as shown in FIG. 4. Interestingly, none of the cysteines are deleted in this clone. Clones DNA48613~~,~~ and DNA48614 ~~and mGFRα3(clone 13) variant~~ have been deposited with ATCC and are assigned ATCC deposit nos. 209752 (Designation: DNA48613-1268)~~,~~ and 209751 (Designation: DNA48614-1268)~~, and _____~~, respectively. A comparison of the nucleic acid sequences encoding DNA48613 with those encoding human GFR.alpha.1 and GFR.alpha.2 is provided in FIGS. 5A-B. The 5' untranslated GFR.alpha.3 sequence immediately upstream of the initiation ATG in the cloned DNA48613 is GCGAGGGGAGCGCGGAGCCCGGCGCCTACAGCTCGCC (SEQ ID NO 21).

Please amend the table beginning at page 58, line 36 as follows:

Material	ATCC Dep. No.	Deposit Date
~~mGFRα3 (clone 13)~~	~~_____~~	~~_____~~
DNA48613	209752	Apr. 7, 1998
DNA48614	209751	Apr. 7, 1998